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U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE ATTORNEY'S DOCKET NUMBER

TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

410.016

U.S. APPLICATION NO. (PCT/PTO) 1390

09/308195

INTERNATIONAL APPLICATION NO

INTERNATIONAL FILING DATE

PRIORITY DATE CLAIMED

PCT/FR97/02336

December 17, 1997

December 23, 1996

TITLE OF INVENTION

METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES

APPLICANT(S) FOR DO/EO/US

THIBAUT et al

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
  2. ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
  3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
  4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
  5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
    - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
    - b. ☐ has been transmitted by the International Bureau.
    - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
  6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
  7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
    - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
    - b. ☐ have been transmitted by the International Bureau.
    - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
    - d. ☐ have not been made and will not be made.
  8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
  9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
  10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).
- Items 11. to 16. below concern other document(s) or information included:
11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
  12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
  13. ☒ A FIRST preliminary amendment.  
☐ A SECOND or SUBSEQUENT preliminary amendment.
  14. ☐ A substitute specification.
  15. ☐ A change of power of attorney and/or address letter.
  16. ☒ Other items or information: Verified Statement Claiming Small Entity Status- Small Business Concern; PCT/IPEA/416; PCT/IPEA/409; PCT/IPEA/408; Annexe; PCT/IPEA/429; PCT/IPEA/428WP; Reponse; Replacement Claims (3 pages); Drawings (7 sheets)

17. ☒ The following fees are submitted:

Basic National Fee (37 CFR 1.492(a)(1)-(5)):  
Search Report has been prepared by the EPO or JPO ..... \$830.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)  
..... \$640.00

No international preliminary examination fee paid to USPTO (37 CFR 1.482)  
but international search fee paid to USPTO (37 CFR 1.445(a)(2)) ..... \$710.00

Neither international preliminary examination fee (37 CFR 1.482) nor  
international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... \$950.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)  
and all claims satisfied provisions of PCT Article 33(2)-(4) ..... \$90.00

ENTER APPROPRIATE BASIC FEE AMOUNT = \$ 970.00

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30  
months from the earliest claimed priority date (37 CFR 1.492(c)).

Claims	Number Filed	Number Extra	Rate
Total Claims	-20 -		X \$22.00
Independent Claims	-3 -		X \$74.00
Multiple dependent claims(s) (if applicable)			+ \$230.00

TOTAL OF ABOVE CALCULATIONS = \$ 970.00

Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement  
must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).

SUBTOTAL = \$ 485.00

Processing fee of \$130.00 for furnishing the English translation later the ☐ 20 ☐ 30  
months from the earliest claimed priority date (37 CFR 1.492(f)).

TOTAL NATIONAL FEE = \$ 485.00

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be  
accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property +

TOTAL FEES ENCLOSED = \$ 525.00

Amount to be:  
refunded \$  
charged \$

- a. ☒ A check in the amount of \$525.00 to cover the above fees is enclosed.
- b. ☐ Please charge my Deposit Account No. \_\_\_\_\_ in the amount of \$ \_\_\_\_\_ to cover the above fees.  
A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any  
overpayment to Deposit Account No. 02-2275. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Bierman, Muserlian and Lucas  
600 Third Avenue  
New York, NY 10016

SIGNATURE

Charles A. Muserlian

NAME

19,683

REGISTRATION NUMBER

**VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS**  
**(37 CFR 1.9(f) & 1.27(c))--SMALL BUSINESS CONCERN**

Docket Number (Optional)

410.016

Applicant or Patentee: Eric THIBAUT and Jean-Loup ROMET-LEMONNESerial or Patent No.: PCT/FR97/02336Filed or Issued: December 17, 1997Title: METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES

I hereby declare that I am

- ☐ the owner of the small business concern identified below:  
☒ an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF SMALL BUSINESS CONCERN I.D.M. IMMUNO-DESIGNED MOLECULESADDRESS OF SMALL BUSINESS CONCERN 172, rue de CharonneF-75011 Paris, FRANCE

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 37 CFR 121.12, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

- ☐ the specification filed herewith with title as listed above.  
☒ the application identified above.  
☐ the patent identified above.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights in the invention must file separate verified statements averring to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization having any rights in the invention is listed below:

- ☐ no such person, concern, or organization exists.  
☒ each such person, concern or organization is listed below.

Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Jean-Loup ROMET-LEMONNETITLE OF PERSON IF OTHER THAN OWNER Executive Vice-PresidentADDRESS OF PERSON SIGNING 172, rue de Charonne, F-75011 Paris, FranceSIGNATURE [Signature] DATE April 14, 1999

09/308195

510 Rec'd PCT/PTO 12 MAY 1999

Our Ref.: 410.016

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: :  
THIBAUT et al :  
PCT/FR97/02336 :  
Serial No.: : PCT Date: December 17, 1997  
Filed: Concurrently Herewith :  
For: METHOD AND SYSTEM FOR QUALITY :  
MANAGEMENT IN THERAPEUTIC :  
PROCESSES :  
600 Third Avenue  
New York, NY 10016

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE CLAIMS:

Claim 3, line 1, cancel "one claims 1 or 2" and insert --claim 1--.

Claims 5 to 8, line 1 of each, claims 12 and 13, line 3 of each, and claim 14, line 2, cancel "any one of the previous claims" and insert --claim 1--.

REMARKS

The amendment is presented to conform the claim dependency to the American practice. The Examiner should examine claims 1 to 14

on the replacement pages and not original claims 1 to 15.

Respectfully submitted,  
BIERMAN, MUSERLIAN AND LUCAS



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Enclosure: Return Receipt Postcard

661-8000

"Method and system for quality management  
in therapeutic processes"

DESCRIPTION

The present invention relates to a process for quality  
5 management in therapeutic processes. It also relates to a  
system for its implementation.

The new therapeutic protocols involved at the level of  
cells and genes require a high level of reliability and  
security owing to the complexity of the operations carried  
10 out, the number of stages and personnel involved in the  
protocol. The quality requirement is even more crucial as  
these new therapies relate to the elementary blocks of human  
beings and are moreover the subject of justified vigilance  
on the part of health authorities. It is moreover essential  
15 to guarantee total tracability of samples.

Cell therapy kits, for example the MAK™ kit produced by  
the company IDM, are currently finalized for supply to the  
laboratories in charge of treating cell samples taken from  
patients for whom clinicians have prescribed this therapeutic  
20 protocol. The cells treated in this way are reinjected into  
these patients.

In these therapeutic processes, both biological elements  
and physical objects are treated: the sample bags each  
associated with a patient and information: data associated  
25 with these bags and which indicate, in particular, the  
operators and the process state of progress.

The stages of treatment of the bags of cells are  
subjected to Standard Operating Procedures (SOPs) which are  
fully codified. Observance of these procedures ensures the  
30 quality of treatment required in order to be approved.  
However, the complexity of these procedures, the  
participation of several entities which are partners in the  
treatment processes, the need to rationalize the management  
of the increasingly automated therapeutic processes and the  
35 wish for vigilance expressed by the health authorities have  
led to the observation that it is not possible to segment  
responsibility for the management of therapeutic process

The document US 5 307 262 describes a process and system for quality management of clinical data related to patients.

The document WO 94 27238 describes a testing system for microbiological specimens, including at least one workstation linked/connected to a database containing information relating to patients and a microbiological database. In particular, this system envisages the attribution of an identification number allowing access to the database and to link each tested specimen with the information relating to the patient concerned, the input of data relative to the test performed on the specimen using screen pages and the provision of a report.

The purpose of the invention is to propose a quality management process which guarantees total consistency in the search for security and tracability throughout the different stages of the therapeutic process.

35 This objective is achieved with a process for the management of quality in a therapeutic process, this therapeutic process comprising the stages of taking cells from a patient, a specific treatment of these cells using a

specific treatment protocol, and reinjection into the patient of said cells treated in this way.

According to the invention, the process comprises:

- stages of identification of the entities involved in the therapeutic process,
- stages of sequential and conditional validation of the stages of the therapeutic process, and
- stages of quality control in which data acquired during said validation stages are processed in order to supply information on the quality of the realization of said therapeutic process, said stages of identification, validation and control being carried out for each batch of samples taken from a given patient.

In this way, with the process according to the invention, it becomes possible to provide checking and follow-up of complex therapeutic processes involving several entities and requiring total tracability.

A major advantage of the quality management process according to the invention in fact resides in the fact that it is based on the idea that a batch is associated with each patient, and that this batch and its associated data must be followed throughout the process. In particular, the standard operating procedures (SOP) can be followed and validated, ensuring a high level of tracability, reliability, and security.

When the quality management process according to the invention is implemented in a therapeutic process involving



several entities, optionally remote, and is associated with a standard operating procedure for preparation comprising a series of functional stages, this process then preferably comprises:

5           - stages of validation respectively associated with each of the functional stages, the passing from one validation stage to the following validation stage being conditional on the results of the processing of data collected during this validation stage, and

10           - a stage of processing of the information and data collected in the different validation stages, in order to issue final certification of a preparation carried out according to the standard operating procedure and/or a list of the anomalies detected during the preparation.

15           In a preferred implementation of the invention, validation of the final certification is conditional on the input of a validation password.

          The quality management process according to the invention is advantageously implemented in the form of  
20           software installed on a data processing system. With each validation stage is associated at least one screen page which can be accessed on the display means of at least one workstation connected to the data processing system.

          Each screen page comprises a coded identification field  
25           for a patient which matches the batch of samples subjected to the standard operating procedure.

          It can advantageously be envisaged for the exit from certain stages of the process to be conditional on printing the screen pages corresponding to these stages.

30           In the case of a quality management process implemented in a preparation laboratory receiving therapeutic kits from at least one operational entity, this process then further comprises stages for monitoring the transfer of these kits.

          When the preparation laboratory deals with a  
35           cytapheresis service, the quality management process further comprises stages for monitoring the receipt of cytapheresis pouches.

According to another aspect of the invention, a quality management system is proposed for the implementation of the process according to the invention. The functions of this quality management system can further be extended to include the management of other sectors of the preparation laboratory involved in the therapeutic process. Moreover, this system is preferably connected to a communications network, open or closed, for exchanging data with other entities involved in a therapeutic process.

The invention relates to a quality management system allowing the setup of other similar therapeutic protocol preparation processes and then their control and management within the same system.

Further features and advantages of the invention will appear in the description below. In the attached drawings, given as non-limitative examples:

- Figure 1 shows a quality management system according to the invention organized around one operator;
- Figure 2 shows a quality management organization involving several therapeutic processes;
- Figure 3 shows the different stages of a therapeutic process with which a quality management process according to the invention is associated;
- Figure 4 shows the essential stages of the software implementing the quality management process according to the invention;
- Figure 5 is a schematic representation of a screen page providing access to all the quality management stages;
- Figure 6 is a schematic representation of a screen page corresponding to a stage of preparation of an autologous serum;
- Figure 7 is a schematic representation of a screen page corresponding to a stage of bacteriological control;
- Figure 8 is a schematic representation of a screen page corresponding to a stage of quality control test result input;
- Figure 9 is a schematic representation of a screen

page corresponding to a stage of retrospective analysis;

- Figure 10 is a schematic representation of a screen page corresponding to a stage of final certification;

5     - Figure 11 is a schematic representation of a screen page corresponding to a stage of listing anomalies; and

- Figure 12 is a schematic representation of a screen page corresponding to a stage of transfer from the preparation laboratory to the treatment centre.

10     There follows a description of an example of implementation of the process according to the invention, in the area of cell therapy.

The parties involved in the operation of the process according to the invention are, with reference to Figure 1:

15     - an entity EX controlling operation of the process according to the invention and distributing the therapeutic kits KT,

- treatment centres CT, CTi, CTn run by clinicians CL, CLi, CLn who, for their patients PA, PAi, PAn, take the initiative of starting therapeutic protocols,

20     - preparation laboratories Ll, Li, Ln which prepare, analyze and pack the products used in these therapeutic protocols,

- cytopheresis services CY, CYi, CYn which take samples from patients and make reinjections into them,

25     - bacteriological testing laboratories CB, CBi, CBn, and optionally collection centres CR separate from the operational entity EX.

30     The main stages of the therapeutic process controlled by the quality management process according to the invention are specified in several examples schematically illustrated in Figure 1.

In a first configuration encountered in the operation of the process according to the invention and described sequentially in Figure 3,

35     - 1/ a clinician CL in charge (0) of a patient PA within a treatment centre CT, issues a diagnosis DI and decides to contact a preparation laboratory Ll in order to start one or

more protocols intended for his patient,

- 2/ this laboratory L1 then contacts the operational entity EX for the therapeutic protocol process for it to supply it with the therapeutic kits corresponding to this protocol,

- 3/ the laboratory L1 also contacts a cytappheresis service CY with a view to organizing taking a plasma sample from the patient; a sample PR is taken from the patient;

- 4/ the laboratory L1 receives the therapeutic kit KT and an associated cytappheresis sheet from the operational entity EX or from a collection centre; the standard operating procedure(s) (SOP's) is/are then initiated,

- 5/ the laboratory L1 receives sample pouches from the cytappheresis service CY;

- 6/ the contents of these pouches are treated (TR) by the laboratory according to a standard operating procedure SOP and under the control of the quality management process according to the invention,

- 7/ then, when a final certification F is granted, the treated pouches accompanied by the necessary documents are sent to the clinician who arranges reinjection RI into the patient,

- 8/ post-reinjection follow-up information is input (7') and forwarded to the operational entity EX.

The operational entity is at the heart of the therapeutic process and manages the quality control and guarantees the tracability which is essential for this type of operation. The quality management process is intimately linked to the operating procedure SOP1 implemented in the laboratory L1, but it can also be involved in the management G of this laboratory.

In another possible operating configuration of the quality management process according to the invention, part of the entities involved in the therapeutic process are integrated on a single site. In this way, the laboratory Li in charge of the preparation can for exemple include the treatment centre CTi and its clinicians CLi in charge of

patients PA<sub>i</sub> and of the cytopheresis services CY<sub>i</sub>, the bacteriological control being carried out by an external laboratory CB<sub>i</sub>. The quality management process according to the invention can then be implemented both to follow up the  
 5 operating procedure SOP<sub>i</sub> and to provide quality management Gi within the other entities CY<sub>i</sub>, CT<sub>i</sub>.

It can also be envisaged for the distribution of the therapeutic kits not to be directly carried out by the operational entity Ex but assigned to a collection centre CR  
 10 with which a preparation laboratory Ln is in contact for the supply of the kits. The quality management process according to the invention then handles the follow-up of the procedure SOP<sub>n</sub> and the management Gn of this preparation laboratory which is also in contact with a bacteriological control  
 15 laboratory CB<sub>n</sub>, a cytopheresis laboratory and one or more treatment centres CT<sub>n</sub> to which the clinicians CL<sub>n</sub> and their patients PA<sub>n</sub> are attached. The operational entity Ex receives from each preparation laboratory the information relating to the quality management of the operating  
 20 procedures and post-reinjection monitoring. This data is processed, analyzed and optionally forwarded to a supervising authority AT.

The process according to the invention can be implemented for the quality management of several therapeutic  
 25 protocols, as illustrated in Figure 2.

Several therapeutic protocols can be operated by an equivalent number of operational entities EX<sub>a</sub>, EX<sub>b</sub> each controlling a network Ra, Rb of preparation laboratories L<sub>a,1</sub>, L<sub>a,2</sub>, L<sub>a,3</sub>, L<sub>a,1</sub>, L<sub>a,1+1</sub>, L<sub>a,N</sub>; L<sub>b,1</sub>, L<sub>b,2</sub>, L<sub>b,3</sub>, L<sub>b,1</sub>, L<sub>b,1+1</sub>, L<sub>b,1+2</sub>, L<sub>b,M</sub>.  
 30 These laboratories carry out preparations for the treatment centres CT of patients PA and are all equipped with software implementing the quality management process according to the invention. The operational entities EX<sub>a</sub>, EX<sub>b</sub> supply the laboratories with therapeutic kits, provide supervision of  
 35 the preparation operations carried out by the laboratories, collect quality management data and report for exemple to a supervising authority AT.

The data processing tools implemented with the quality management process can furthermore provide other control and processing functions, as illustrated in the diagram in Figure 4. In this way, the quality management process according to the invention offers the operator a command bar BC which provides access in particular to the following features:

- a Guide feature, which comprises a set of information on the techniques implemented in the therapeutic process, in particular in the form of animated sequences SA, SA1, SA2,..., SAm or of video sequences;
- a full sequential follow-up of the standard operating procedures (SOPs) which constitute the heart of the software embodying the process according to the invention; this software element EL comprises in particular a set of screen pages PO, PE1,..., PEn which are consulted sequentially and filled in by the operator;
- management and archiving DB of the data collected during the operation of the quality management process;
- management LM of the preparation laboratory which can include stock management SM, personnel management PM including in particular training requirements and ongoing appraisal of this personnel, input/output management OM, and automated management GM of the standard operating procedures;
- a network feature NM for managing communications between the laboratory L1 and the other entities involved in the therapeutic protocols, in particular with bacteriological control laboratories CB, with treatment centres CT, with cytapheresis services CY, an operational entity EX, a collection centre CR and a connection XT to other networks.

There follows a description of the main stages of the quality management process according to the invention, with reference to the corresponding screen pages encountered by operators. It is here considered that the quality management process according to the invention is implemented in the form of software installed on an I.T. workstation in a preparation laboratory.

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date D, a module RM indicating the details of the laboratory responsible for the preparation and the batch number LN, and a module BS containing the data relating to the bacteriological control, in particular the address AB of the laboratory in charge of the bacteriological control, an indication OB of the control operator, the results TB of a set of bacteriological control tests and the date DB of these tests. This screen page EB further comprises an indication AL that printing of this screen page is mandatory. A print command icon PR is provided for this purpose.

When all the stages of the standard operating procedure SOP have been executed, a screen page ER lists all the results of the quality tests which must be entered by the operator. This screen page ER comprises a similar header containing a title PR, a reminder of the patient code CP and the operation date D, and a table listing a series of quantitative tests CT with each of which is associated a "result" field RE which must be completed by the operator, and a "standards" field containing the maximum and minimum values constituting the standards. An icon BA allows the operator to return to the previous screen pages.

A retrospective analysis screen page EA (Fig. 9) must be completed by the operator once the treated cells have been reinjected. This screen page EA contains a header including a stage title RA, the patient code CP and the date D, and a table listing, for a set EXA of tests PH, CX, CS, BS carried out after reinjection, the results RE which must be entered by the operator and, opposite each result, the corresponding standard NO.

Final certification of a preparation is obtained from a specific screen page EC (Fig. 10) which, in addition to the identification header containing a title FC, the patient code CP and the date D, comprises a declaration CF of final certification providing significant quantitative and qualitative results RF specific sizes and physiological characteristics CF: number of cells, viability, percentage, sterility. There follows a declaration of final

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and fax numbers TL, FA and the name PI of the person in charge of this treatment.

5 A message MA warns the operator that this screen page must be printed, further comprising, for example at the bottom of the page, information relating to transmission and reception operations. In this way, the transmission EN and reception ER lines must be completed by the operator for the following fields: dates DS, DR; times TS, TR and persons in charge PS, PT.

10 Of course, the invention is not limited to the examples which have just been described and numerous developments can be added to these examples without exceeding the scope of the invention. In this way, this process can be applied to the control and follow-up of quality in many fields other than  
15 that of cell therapy. It can moreover be integrated into laboratory automation processes. The process according to the invention also takes account of current concerns relating to biological vigilance and pharmacological vigilance.

ARJY

CLAIMS

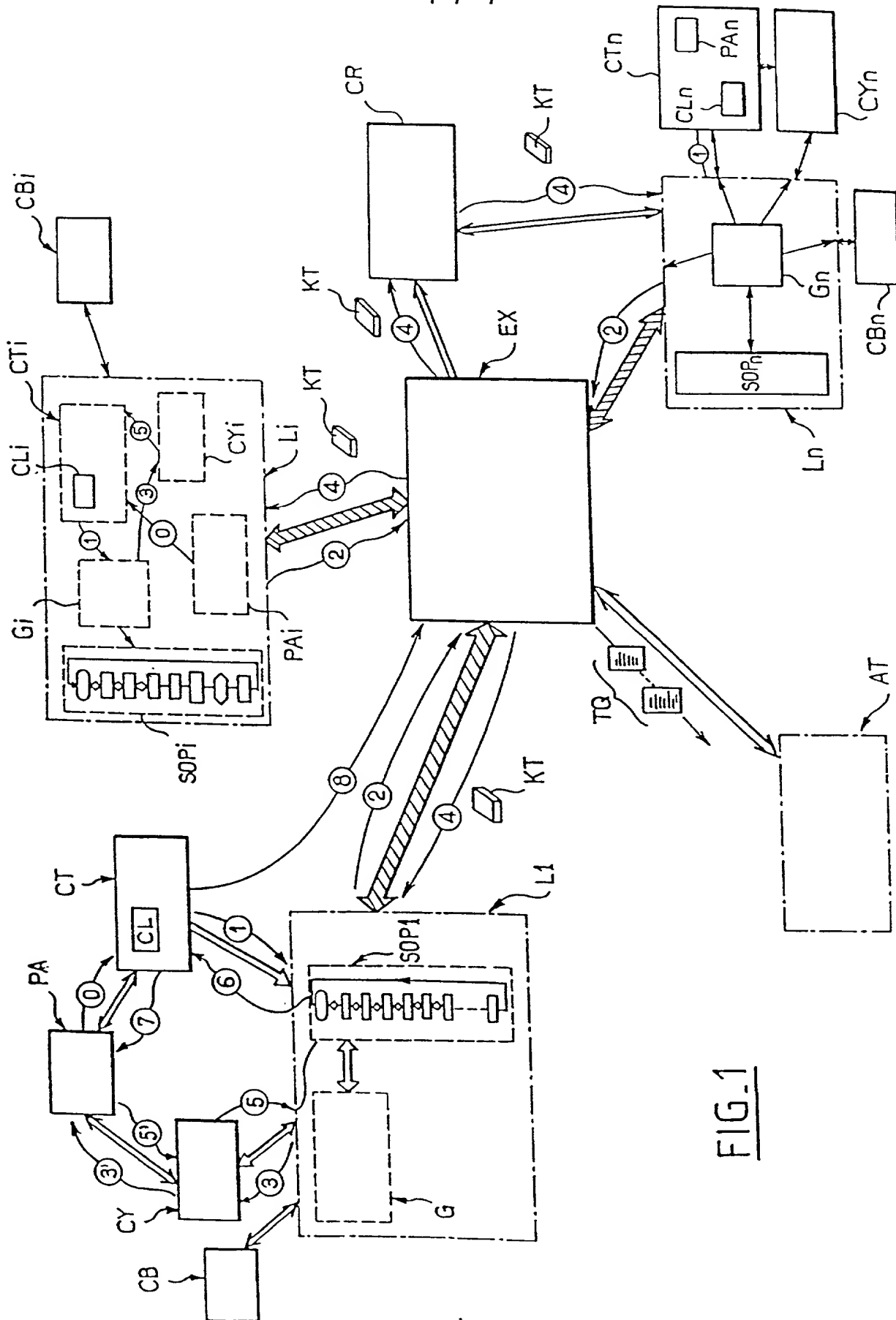
1. Process for the processing of information used for the management of quality in a therapeutic process, this  
5 therapeutic process comprising the operations of taking cells (PR) from a patient (PA), specific treatment operations on these cells using a specific treatment protocol, and a reinjection operation into the patient of said cells treated in this way, these operations of taking cells, treatment and  
10 reinjection being subjected to a standard operating procedure for preparation (SOP) comprising a series of functional stages, characterized in that it comprises, for each batch of samples taken from a given patient:
- 15 - for each functional stage, a stage of sequential and conditional validation (VA) of said stage, the passing from one validation stage to the following validation stage being conditional on the results of the processing of data collected during this validation stage, and  
20 - a stage of processing of the information and data collected in the different validation stages, in order to issue final certification (CF) of a preparation carried out according to the standard operating procedure and/or a list of the anomalies detected during this preparation.
- 25
2. Process according to claim 1, characterized in that validation of the final certification is conditional on the input of a validation password.
- 30
3. Process according to one claims 1 or 2, implemented in a data processing system, characterized in that with each validation stage is associated at least one screen page (PO, Pei, EP, EA, EC, EI) which can be accessed on the display means of at least one workstation connected to said data  
35 processing system.
4. Process according to claim 3, characterized in that each

screen page comprises a coded identification field for a patient which matches the batch of samples subjected to the standard operating procedure.

- 5 5. Process according to any one of the previous claims, characterized in that the exit from certain stages (RA) of said process is conditional on printing the screen pages (EA) corresponding to these stages.
- 10 6. Process according to any one of the previous claims, implemented in a preparation laboratory receiving therapeutic kits from at least one operational entity (EX), characterized in that it further comprises stages for monitoring the transfer of these kits.
- 15 7. Process according to any one of the previous claims, implemented in a preparation laboratory which deals with a cytappheresis service, characterized in that it further comprises stages for monitoring the receipt of cytappheresis
- 20 pouches.
8. Process according to any one of the previous claims, implemented in a preparation laboratory which deals with a control laboratory, in particular a bacteriological control
- 25 laboratory, characterized in that it further comprises stages for processing the results of control tests carried out on each batch of samples.
9. System for the processing of information used for the
- 30 management of quality in a therapeutic process, this therapeutic process comprising the operations of taking cells (PR) from a patient (PA), specific treatment operations on these cells using a specific treatment protocol (SOP), and a reinjection operation (RI) into the patient of said cells
- 35 treated in this way, these operations of taking cells, treatment and reinjection being subjected to a standard operating procedure for preparation comprising a series of

functional stages (TR),  
characterized in that it comprises, for each batch of samples  
taken from a given patient:

- for each functional stage, a means of sequential and  
5 conditional validation (VA) of said stage, the passing from  
one validation stage to the following validation stage being  
conditional on the results of the processing of data  
collected during this validation stage, and
  - a means of processing of the information and data collected  
10 in the different validation stages, in order to issue final  
certification (CF) of a preparation carried out according to  
the standard operating procedure and/or a list of the  
anomalies detected during the preparation.
- 15 10. System according to claim 9, implemented in a preparation  
laboratory, characterized in that it is further designed to  
execute management tasks (GN) within this laboratory.
- 20 11. System according to claim 9, characterized in that it is  
connected to a communications network in order to exchange  
data with other entities (CTn, Ln, Cyn, CRn, CB) involved in  
a therapeutic process.
- 25 12. Application of the process and of the information  
processing system used for quality management according to  
any one of the previous claims to cell therapy protocols.
- 30 13. Application of the process and of the information  
processing system used for quality management according to  
any one of the previous claims to gene therapy protocols.
- 35 14. Application of the process and of the quality management  
system according to any one of the previous claims, allowing  
ongoing training of the operator and/or the monitoring of his  
or her level of knowledge.



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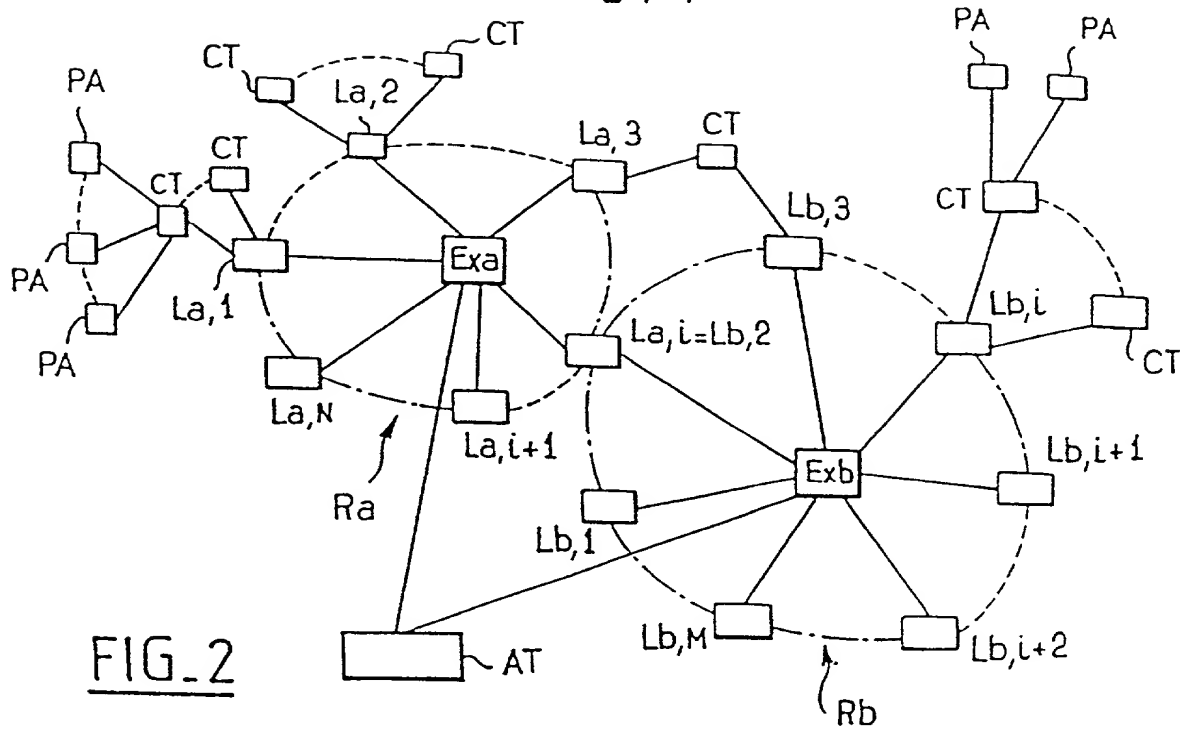


FIG. 2

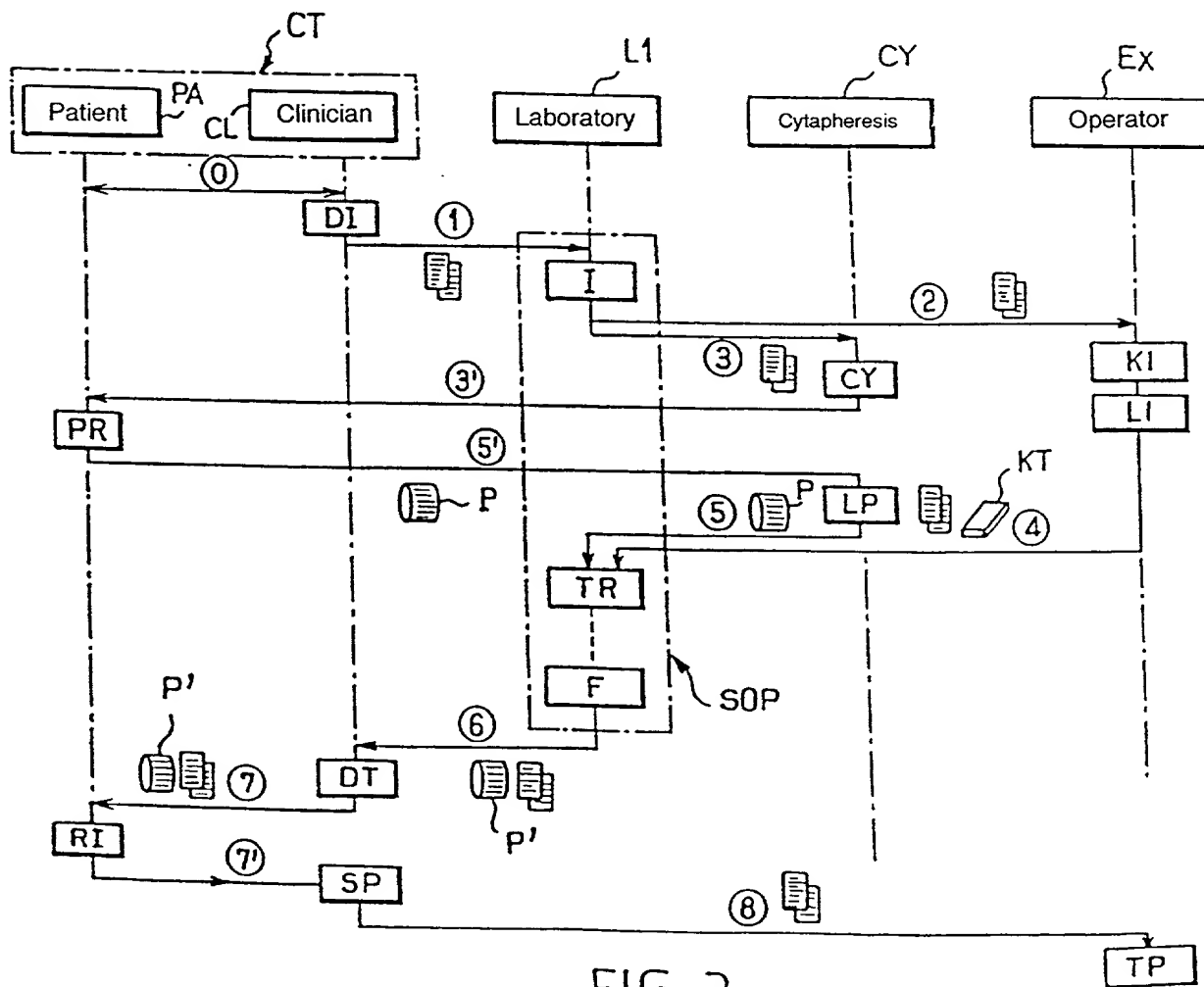


FIG. 3



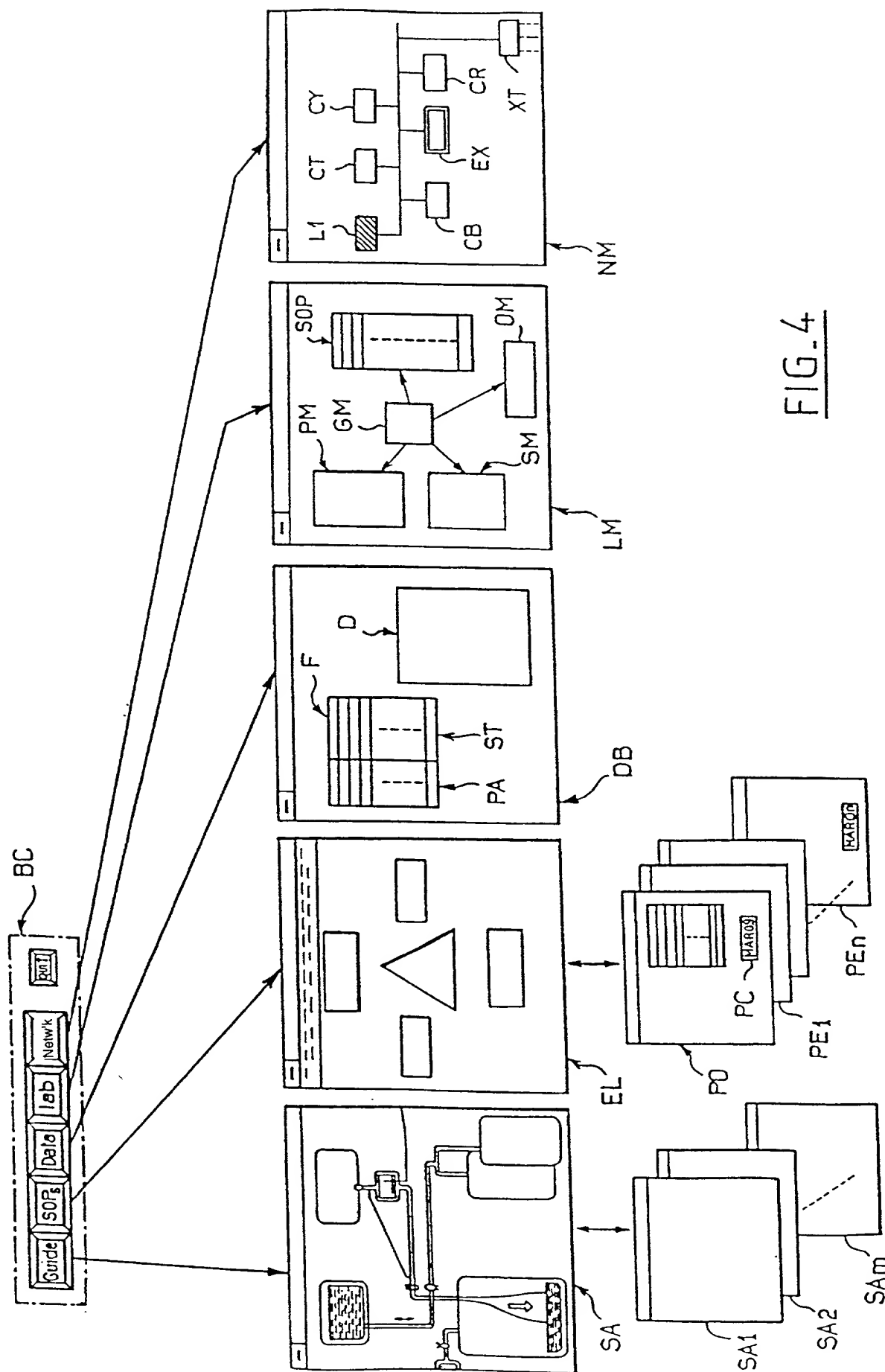


FIG. 4

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PO

RM

LA

AD

TL FA

EM

CL

DD

DF

ST

LN MAR 09

BC

E1

E2

E<sub>i</sub>

E<sub>n</sub>

E

MAR 09

CP

CA

FIG. 5

PEI

EP

CP MAR 09

D

S1

S2

S<sub>j</sub>

S<sub>n</sub>

VA

CA

FIG. 6

ST

EC

CP

MAR 09

D

EB

RM

LA

AD

TL

FA

EM

LN

MAR 09

BS

AB

OB

TB

DB

AL

PR

CA

FIG. 7

CP

MAR 09

PR

D

ER

CT	RE	NO
	%	
	%	
	%	

BA

VA

CA

FIG. 8

Diagram of the control panel of the "Mikro-1" computer. The panel features a central table with three columns: EXA, RE, and NO. The EXA column lists the program counter (PH), instruction register (CX), status register (CS), and basic register (BS). The RE column displays percentage values. The NO column displays dashes. To the right of the table are three buttons labeled VA, CA, and a third unlabeled button. Above the table are three input fields labeled RA, CP (containing "MAR 09"), and D. An arrow labeled EA points to the left side of the table.

EXA	RE	NO
PH		—
—	%	—
—	%	—
—	%	—
—	%	—
—	%	—
CX	%	—
CS	%	—
BS	- -	—

FIG. 9

The diagram shows a control panel with the following elements:

- FC**: A rectangular button at the top center.
- D**: A three-segment indicator to the right of the FC button.
- CP**: A rectangular button containing the text "MAR 09" below the FC button.
- CF**: A large rectangular button with horizontal lines, located below the CP button.
- RF**: A rectangular button with horizontal lines, located to the right of the CF button.
- AI**: An octagonal button with an exclamation mark and a horizontal bar, located to the right of the RF button.
- DC**: A rectangular button located below the CF and RF buttons.
- Y** and **N**: Two small square buttons located to the right of the DC button.
- EC**: A label with a curved arrow pointing to the left edge of the panel.
- PC**: A button with a speech bubble icon, located at the bottom left.
- PR**: A button with a speech bubble icon, located at the bottom center.
- VA**: A square button, located at the bottom right.
- CA**: A square button with a diamond and arrow icon, located at the bottom right.

FIG. 10

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EI

LI ~ [ ]

CP [ MAR 09 ] [ ] [ ] ~ D

ST ~ [ ]

LN ~ [ ]

☐ [ I1 ]

☐ [ I2 ]

☐ [ I3 ]

☐ [ I4 ]

NI [ ] [ ] [ ]

TI [ ] [ ] [ ]

[ ] IN

[ ] PR

[ ] CA

FIG. 11

ET

ST [ ]

CP [ MAR 09 ] D [ ] [ ] [ ]

LAB		TC	
LA [ ]		TR [ ]	
AD [ ]		AD [ ]	
TL [ ]	FA [ ]	TL [ ]	FA [ ]
[ ]		PI [ ]	
CL [ ]		[ ]	MA [ ]
DB [ ] [ ] [ ]			
DE [ ] [ ] [ ]			
LN [ ] [ ] [ ]			
AN [ ] [ ] [ ]			

EN [ ] [ ] [ ] DS [ ] [ ] [ ] TS [ ] [ ] [ ] PS [ ] [ ] [ ]

ER [ ] [ ] [ ] DR [ ] [ ] [ ] TR [ ] [ ] [ ] PT [ ] [ ] [ ]

[ ] PR

[ ] VA

[ ] CA

FIG. 12

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# DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

☒ Declaration Submitted with Initial Filing OR ☐ Declaration Submitted after Initial Filing

Attorney Docket Number	410.016
First Named Inventor	Eric THIBAUT et al
COMPLETE IF KNOWN	
Application Number	PCT/FR97/02336
Filing Date	December 17, 1997
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES

(Title of the Invention)

the specification of which

☐ is attached hereto  
OR

☒ was filed on (MM/DD/YYYY) 12/17/97

as United States Application Number or PCT International

Application Number PCT/FR97/02336 and was amended on (MM/DD/YYYY) (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56

I hereby claim foreign priority benefits under Title 35 United States Code §119 (a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?	
96/15839	France	12/23/96	<input type="checkbox"/>	YES	NO
PCT/FR97/02336	PCT	12/17/97	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto.

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below

Application Number(s)	Filing Date (MM/DD/YYYY)	<input type="checkbox"/> Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

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## DECLARATION

I hereby claim the benefit under Title 35, United States Code § 120 of any United States application(s), or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number	Name	Registration Number
Bierman, Muserlian and Lucas	18,818		
Jordan B. Bierman	18,629		
Charles A. Muserlian	19,683		
Donald C. Lucas	31,275		

☐ Additional registered practitioner(s) named on a supplemental sheet attached hereto.

Direct all correspondence to:

Name	Charles A. Muserlian		
Address	Bierman, Muserlian and Lucas		
Address	600 Third Avenue		
City	New York	State	NY
ZIP	10016		
Country	U.S.A.	Telephone	(212) 661-8000
Fax	(212) 661-8002		

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor:

☐ A petition has been filed for this unsigned inventor

Given Name	Eric	Middle Initial		Family Name	THIBAUT	Suffix e.g. Jr.	
Inventor's Signature					Date	26/04/1999	
Residence: City	Jouars-Pontchartrain	State		Country	France	Citizenship	France
Post Office Address	5, chemin des Anjoux F-78760 Jouars-Pontchartrain, France						
Post Office Address							
City	Jouars-Pontchartrain	State		Zip	F-78760	Country	France

☒ Additional inventors are being named on supplemental sheet(s) attached hereto

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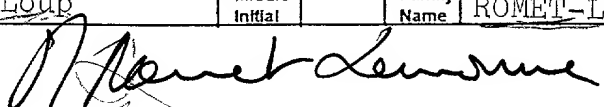
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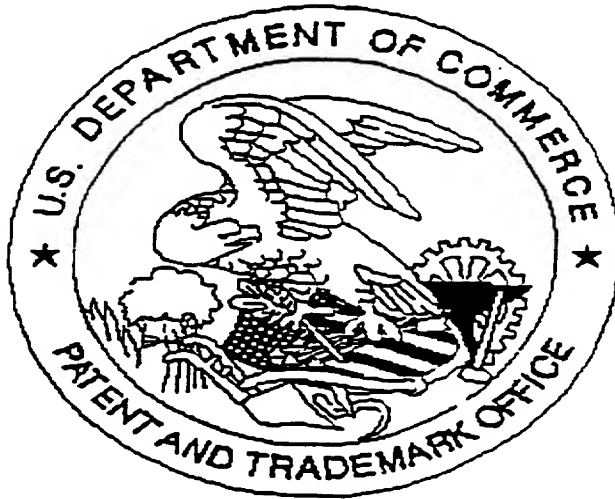
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<b>DECLARATION</b>	<b>ADDITIONAL INVENTOR(S) Supplemental Sheet</b>
--------------------	--

Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Jean-Loup	Middle Initial		Family Name	ROMET-LEMONNE	Suffix	
Inventor's Signature					Date	04/16/1994	
Residence: City	Paris	State		Country	France	Citizenship	France
Post Office Address		8, rue de Hesse, F-75003 Paris, France					
Post Office Address							
City	Paris	State		Zip	F-75003	Country	France
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name		Middle Initial		Family Name		Suffix	
Inventor's Signature					Date		
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
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Inventor's Signature					Date		
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name		Middle Initial		Family Name		Suffix	
Inventor's Signature					Date		
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name		Middle Initial		Family Name		Suffix	
Inventor's Signature					Date		
Residence: City		State		Country		Citizenship	
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